

**CLAIMS**

1. An isolated peptide fragment of a natural cytotoxicity receptor (NCR) of natural killer (NK) cells, active fragments, analogs or derivatives thereof, the peptide fragment capable of binding to a membrane-associated biomolecule of a tumor cell, the biomolecule comprising at least one sulfated polysaccharide, said biomolecule serving as the binding site of the NCR mediating the lysis of tumor cells by NK cells, with the proviso that said peptide is other than a full length NCR polypeptide or an isolated NCR extracellular domain.
2. The peptide fragment of claim 1 comprising about 7 to about 120 contiguous amino acids.
3. The peptide fragment of claim 1 comprising about 8 to about 100 contiguous amino acids.
4. The peptide fragment of claim 1 comprising less than about 50 contiguous amino acids.
5. The peptide of claim 1, wherein the peptide is a fragment of NCR selected from NKp44, NKp30 and NKp46.
6. The peptide of claim 5, wherein the peptide is a fragment of the D2 domain of NKp46 is selected from SEQ ID No:1 and SEQ ID No:2.
7. The peptide of claim 5, wherein said peptide is a fragment of NKp30 selected from SEQ ID No:3 and SEQ ID No:4.
8. The peptide of claim 5, wherein said peptide is a fragment of NKp44 having SEQ ID No: 5.
9. The peptide of claim 1, wherein said membrane-associated biomolecule is selected from a glycosaminoglycan and a proteoglycan.
10. The peptide of claim 9, wherein the glycosaminoglycan is selected from heparin, heparan sulfate and dermatan sulfate.
11. The peptide of claim 9, wherein the proteoglycan is heparan sulfate proteoglycan selected from a glypican and a syndecan.

- 5 12. A pharmaceutical composition comprising an isolated peptide fragment of a natural cytotoxicity receptor (NCR) of natural killer (NK) cells, active fragments, analogs or derivatives thereof, the peptide fragment capable of binding to a membrane-associated biomolecule of a tumor cell, the biomolecule comprising at least one sulfated polysaccharide, said biomolecule serving as the binding site of the NCR mediating the lysis of tumor cells by NK cells.
13. The pharmaceutical composition of claim 12, the isolated peptide fragment comprising about 7 to about 120 contiguous amino acids.
- 10 14. The pharmaceutical composition of claim 12, the isolated peptide fragment comprising about 8 to about 100 contiguous amino acids.
- 15 15. The pharmaceutical composition of claim 12, the isolated peptide fragment comprising less than about 50 contiguous amino acids.
16. The pharmaceutical composition of claim 12, wherein the peptide is a fragment of NCR selected from NKp44, NKp30 and NKp46.
17. The pharmaceutical composition of claim 16, wherein the peptide is a fragment of the D2 domain of NKp46 selected from SEQ ID No: 1 and SEQ ID No: 2.
- 20 18. The pharmaceutical composition of claim 16, wherein said peptide is a fragment of NKp30 selected from SEQ ID No: 3 and SEQ ID No: 4.
19. The pharmaceutical composition of claim 16, wherein said peptide is a fragment of NKp44 having SEQ ID No: 5.
- 25 20. The pharmaceutical composition of claim 12, wherein said membrane-associated biomolecule is selected from a glycosaminoglycan and a proteoglycan.
21. The pharmaceutical composition of claim 20, wherein the glycosaminoglycan is selected from heparin, heparan sulfate and dermatan sulfate.
22. The pharmaceutical composition of claim 20, wherein the proteoglycan is heparan sulfate proteoglycan selected from a glypican and a syndecan.

23. An antibody that recognizes an epitope on a target membrane-associated biomolecule of a tumor cell, the biomolecule comprising at least one sulfated polysaccharide, said biomolecule mediating the lysis of tumor cells by NK cells via the natural cytotoxicity receptor (NCR).
- 5 24. The antibody of claim 23, wherein the membrane-associated biomolecule is selected from a glycosaminoglycan and a proteoglycan.
25. The antibody of claim 24, wherein the glycosaminoglycan is selected from heparin, heparan sulfate and dermatan sulfate.
- 10 26. The antibody of claim 24, wherein the proteoglycan is heparan sulfate proteoglycan selected from a glypican and a syndecan.
- 15 27. A pharmaceutical composition comprising an antibody that recognizes an epitope on a target membrane-associated bio-molecule of a tumor cell, the biomolecule comprising at least one sulfated polysaccharide, said biomolecule mediating the lysis of tumor cells by NK cells via the natural cytotoxicity receptor (NCR).
28. The pharmaceutical composition of claim 27, wherein the membrane-associated biomolecule is selected from a glycosaminoglycan and a proteoglycan.
- 20 29. The pharmaceutical composition of claim 28, wherein the glycosaminoglycan is selected from heparin, heparan sulfate and dermatan sulfate.
30. The pharmaceutical composition of claim 28, wherein the proteoglycan is heparan sulfate proteoglycan selected from a glypican and a syndecan
- 25 31. A method of targeting a tumor cell in a subject in need thereof via an NCR-dependent mechanism, said method comprising administering to the subject a pharmaceutical composition according to claims 12 or 27.
32. The method of claim 31, wherein the peptide is a fragment of NCR selected from NKp44, NKp30 and NKp46.
33. The method of claim 32, wherein the peptide is a fragment of the D2 domain of NKp46 is selected from SEQ ID No: 1 and SEQ ID NO:2

34. The method of claim 32, wherein the peptide is a fragment of NKp30 selected from a peptide having SEQ ID No. 3 and SEQ ID No. 4.
35. The method of claim 32, wherein the peptide is a fragment of NKp44 having SEQ ID No. 5.
- 5 36. The method of claim 32, wherein the membrane-associated bio-molecule is a glycosaminoglycan or a proteoglycan.
37. The method of claim 36, wherein the glycosaminoglycan is selected from heparin, heparan sulfate and dermatan sulfate.
38. The method of claim 36 wherein the proteoglycan is a heparan sulfate proteoglycan selected from a glypican and a syndecan.
- 10 39. A method of identifying peptides derived from NCR which are capable of binding to a membrane-associated sulfated polysaccharide of a tumor cell, comprising the steps of:
- a. providing a set of candidate peptides;
  - 15 b. contacting the peptides with a tumor cell;
  - c. determining the binding of said peptides to said tumor cell; and
  - d. isolating said bound peptides.
40. An antibody capable of blocking the binding of NK cells via NCR to membrane-associated sulfated polysaccharide bio-molecules in a cell, thereby
- 20 inhibiting NCR-dependent cell lysis associated with autoimmunity.